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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,514	04/30/2001	K. Roger Aoki	D2929CON	3428

33197 7590 01/13/2005

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,514	AOKI ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,17-25 and 29-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,17-25 and 29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and response filed October 27, 2004 are acknowledged. Claims 1 and 17 have been amended. Claims 10-16, and 26-27 have been cancelled. Claims 28-33 have been added.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

3. In view of Applicant amendment the following rejections are withdrawn:

a) rejection of claims 28-29 under 35 U.S.C. 103(a), pages 3-4, paragraph 5 of the previous Office action.

b) rejection of claims 1-9 and 17-26 under 35 U.S.C. 112 first paragraph, pages 5-6, paragraph 6 of the previous Office action.

c) rejection of claims 1-9 and 17-26 under 35 U.S.C. 112, second paragraph, page7, paragraph 7 of the previous Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-9 are rejected under 35 U.S.C. 103(a) as unpatentable over Ludlow et al et al *(The New England Journal of Medicine, Vol. 326(5), January 1992)* in view of Simpson *(Pharmacological Reviews, Vol. 33(3), pages 155-188, 1991)* and in further view of Jankovic et al *(The New England Journal of Medicine, Vol. 324, pages 1186-1194, 1991).*

Claims 1-9 are drawn to a method of treating a patient suffering from a neuromuscular disorder or condition.

Ludlow et al teach the treatment of neuromuscular disorders and conditions in patients with torticollis and oromandibular dystonia by intramuscular injection with botulinum toxin F after these patients have been treated with botulinum toxin A and they had developed antibodies to toxin A (page 350, col. 1)

Ludlow et al do not teach the other serotypes that are claimed.

Simpson et al teach the pharmacological structure and activity of each of the claimed serotypes, stating that there are all various strains of *C. botulinum* and are

antigenically distinct and they all depress neurogenic release of acetylcholine (pages 155-156, 167 and 180).

Jankovic et al teach the use of botulinum toxin A to treat a number of neurological disorders. Jankovic et al teach that the toxin has the possibility of being blocked by antibodies and as such the treatment becomes ineffective after repeated injections of the toxins as anti-botulinum toxin antibodies developed (page 1189). Jankovic et al states that "it is likely that patients with antibodies against botulinum toxin will respond to injections with other botulinum toxins that are immunologically distinct from type A". Jankovic et al further teach that "any muscle spasm can be temporarily relieved by treatment with the toxin because botulinum toxin acts on the final common pathway".

It would be *prima facie* obvious at the time the invention was made to administer botulinum toxin type F in combination with botulinum toxin type A because the patients had developed antibodies to toxin A, Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct. Therefore, it would it would have been obvious to one of ordinary skill in the art to extend the teachings of Ludlow et al of administering toxin F after toxin A to other serotypes and to administer other serotypes after A as claimed with a reasonable expectation that serotypes other than type F will treat the types of neuromuscular disorders as demonstrated by Ludlow et al. It would be expected barring evidence to the contrary

that the combinations of serotypes of botulinum toxins would be effective in treating patients with neuromuscular disorders because Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct.

5. Claims 17-25 and 28-33 are rejected under 35 U.S.C. 103(a) as unpatentable over Ludlow et al et al *(The New England Journal of Medicine, Vol. 326(5), January 1992)* in view of Simpson *(Pharmacological Reviews, Vol. 33(3), pages 155-188, 1991)* and in further view of Jankovic et al *(The New England Journal of Medicine, Vol. 324, pages 1186-1194, 1991).*

Claims 17-25 and 28-33 are drawn to a composition suitable for treating a patient suffering from a neuromuscular disorder or condition comprising a therapeutically effective amount of at least two neurotoxins.

Ludlow et al teach a composition comprising botulinum toxin type F used in the treatment of patients with torticollis and oromandibular dystonia after these patients have been treated with botulinum toxin A and they had developed antibodies to toxin A (page 350, col. 1)

Ludlow et al do not teach the other serotypes that are claimed.

Simpson et al teach the pharmacological structure and activity of each of the claimed serotypes, stating that there are all various strains of *C. botulinum* and are

antigenically distinct and they all depress neurogenic release of acetylcholine (pages 155-156, 167 and 180).

Jankovic et al teach the use of botulinum toxin A to treat a number of neurological disorders. Jankovic et al teach that the toxin has the possibility of being blocked by antibodies and as such the treatment becomes ineffective after repeated injections of the toxins as anti-botulinum toxin antibodies developed (page 1189). Jankovic et al states that "it is likely that patients with antibodies against botulinum toxin will respond to injections with other botulinum toxins that are immunologically distinct from type A". Jankovic et al further teach that "any muscle spasm can be temporarily relieved by treatment with the toxin because botulinum toxin acts on the final common pathway".

It would be *prima facie* obvious at the time the invention was made to add botulinum toxin type F with botulinum toxin type A because the patients had developed antibodies to toxin A, Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct. Therefore, it would it would have been obvious to one of ordinary skill in the art to extend the teachings of Ludlow et al of administering toxin F after toxin A to other serotypes and to administer other serotypes after A as claimed with a reasonable expectation that serotypes other than type F will treat the types of neuromuscular disorders as demonstrated by Ludlow et al. It would be expected barring evidence to the contrary, that the combinations of serotypes of

botulinum toxins would be effective in treating patients with neuromuscular disorders because Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct.

Status of Claims

6. No claims allowed.

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
January 5, 2004

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